

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1-30. Canceled

31. (Newly added) A method of isolating at least one anti-ligand to at least one target ligand comprising the steps of:

- (i) providing a library of anti-ligands;
- (ii) providing an amount of a first subtractor ligand;
- (iii) providing an amount of a second target ligand;
- (iv) determining amounts of first subtractor and second target ligands using one or more equations derived from the universal law of mass action  $\frac{[C]^c [d]^d}{[A]^a [B]^b} = K_{eq}$ ,

where:

A, B, C & D = are the participants in the reaction (reactants and products)  
 a, b, c, & d = the coefficients necessary for a balanced chemical equation

so as to permit isolation of at least one anti-ligand to at least one target ligand;

- (v) providing the amount of the first subtractor ligand determined in step (iv);
- (vi) providing the amount of the second target ligand determined in step (iv);
- (vii) providing separation means for isolating anti-ligand bound to the second target ligand from anti-ligand bound to the first subtractor ligand;
- (viii) exposing the library of (i) to the ligands of (v) and (vi) to permit binding of anti-ligands to ligands; and
- (ix) isolating the anti-ligand bound to the second target ligand with the separation means.

32. (Newly added) A method of isolating at least one anti-ligand to at least one target ligand comprising the steps of:

- (i) providing data set(s) describing a library of anti-ligands;
- (ii) providing data set(s) describing a first subtractor ligand;
- (iii) providing data set(s) describing a second target ligand;
- (iv) automatically determining amounts of the first subtractor and second target ligands using one or more equations derived from the universal law of mass action
$$\frac{[C]^c[d]^d}{[A]^a[B]^b} = K_{eq},$$

where:

A, B, C & D = are the participants in the reaction (reactants and products)  
a, b, c, & d = the coefficients necessary for a balanced chemical equation  
so as to permit isolation of at least one anti-ligand to at least one target ligand

- (v) providing the amount of the first subtractor ligand determined in step (iv);
- (vi) providing the amount of the second target ligand determined in step (iv);
- (vii) providing the library of anti-ligands described by the data-set of step (i);
- (viii) providing separation means for isolating anti-ligand bound to the second target ligand from anti-ligand bound to the first subtractor ligand;
- (ix) exposing the library of (vii) to the ligands of (v) and (vi) to permit binding of anti-ligands to ligands; and
- (x) isolating the anti-ligand bound to the second target ligand with the separation means.

33. (Newly added) A method as claimed in Claim 32 wherein step (iv) and at least one of steps (v), (vi), (vii) (ix) and (x) are performed automatically.

34. (Newly added) A method as claimed in one of Claims 31, 32 or 33 comprising a further step of releasing the anti-ligand from the second target ligand.

35. (Newly added) A method as claimed in Claim 31 or 32 whereby steps (ii) to (ix) are repeated one or more times.

36. (Newly added) A method as claimed in claim 31 or 32 wherein the amount of one of the first subtractor or second target ligand is provided in excess of the amount of the other of the first subtractor or second target ligand.

37. (Newly added) A method as claimed in Claim 36 where the excess of ligand is of 10 to 100 fold.

38. (Newly added) A method as claimed in Claims 31 or 32 wherein the equation of (iv) is

$$bA = \frac{(A + T + (K_d)x(CxV))}{2} - \sqrt{\frac{(A + T + (K_d)x(CxV))^2}{4} - AxT}$$

where

bA = Bound anti-ligand

A = Total number of anti-ligand

T = Total number of ligands

C = Avogadro's constant ( $6.022 \times 10^{23}$  particles/mole)

V = Reaction volume (litres)

$K_d$  = Equilibrium dissociation constant

39. (Newly added) A method as claimed in Claims 31 or 32 wherein the equation of (iv) is:

$$bA = \left\{ \frac{(A + T + (K_d)x(CxV))}{2} - \sqrt{\frac{(A + T + (K_d)x(CxV))^2}{4} - AxT} \right\} x \left\{ \frac{(T_p x C_p)}{((T_p x C_p) + (T_s x C_s))} \right\}$$

where

bA<sub>p</sub> = Bound anti-ligand

T<sub>p</sub> = The number of ligands on C<sub>p</sub>

T<sub>s</sub> = The number of ligands on C<sub>s</sub>

C<sub>p</sub> = The number of target ligand constructs

$C_s$  = The number of subtractor ligand constructs

A = Total number of anti-ligand

T = Total number of ligands

C = Avogadro's constant ( $6.022 \times 10^{23}$  particles/mole)

V = Reaction volume (litres)

$K_d$  = Equilibrium dissociation constant

40. (Newly added) A method as claimed in Claim 31 or 32 wherein the separation means are selected from at least one of a solid support, cell membrane and/or portions thereof, synthetic membrane, beads, chemical tags and free ligand.
41. (Newly added) A method as claimed in Claim 40 whereby the separation means are cell membranes and/or portions thereof.
42. (Newly added) A method as claimed in Claim 41 whereby the first subtractor and second target ligands are fixed to and/or incorporated within separate cell membranes and/or portions thereof.
43. (Newly added) A method as claimed in Claims 31 or 32 whereby the separation means of the first subtractor and second target ligands have a different density.
44. (Newly added) A method as claimed in Claim 43 wherein the separation means of the first subtractor ligand is of a lower density than the separation means of the second target ligand.
45. (Newly added) A method as claimed in Claim 44 wherein the separation means of the first subtractor ligand is a membrane vesicle.
46. (Newly added) A method as claimed in Claim 44 wherein the separation means of the second target ligand is a whole cell membrane.
47. (Newly added) A method as claimed in Claim 31 or 32 whereby the isolation of anti-ligand bound to second target ligand is performed by at least one of density centrifugation, solid support sequestration, magnetic bead sequestration, chemical tag binding and aqueous phase partitioning.

48. (Newly added) A method as claimed in Claim 47 whereby the isolation step is performed by density centrifugation.
49. (Newly added) A method as claimed in Claim 48 wherein the density centrifugation is performed using a sucrose-polymer gradient.
50. (Newly added) A method as claimed in Claim 31 or 32 wherein the library of step (i) is a display library comprising a plurality of library members which display anti-ligands.
51. (Newly added) A method as claimed in Claim 50 wherein the library is a phage display library.
52. (Newly added) A method as claimed in Claim 31 or 32 wherein the subtractor and target ligands are independently at least one from antigens; receptor ligands; and enzyme targets that comprise at least one selected from carbohydrate; protein; peptide; lipid; polynucleotide; inorganic molecules and conjugated molecules.
53. (Newly added) A method as claimed in Claim 31 or 32 wherein the library of anti-ligands is composed of at least one selected from antibodies, and antigen binding variants, derivatives or fragments thereof; scaffold molecules with engineered variable surfaces; receptors; and enzymes.
54. (Newly added) A method as claimed in Claim 31 or 32 comprising a further step of exposing the ligand and its separation means to a stimulus which influences the expression of target ligands on said ligand constructs.
55. (Newly added) A method for preparing a pharmaceutical composition which comprises, following the identification of an anti-ligand with desired characteristics by a method according to Claim 31 or 32, adding said anti-ligand to a pharmaceutically acceptable carrier.
56. (Newly added) A pharmaceutical composition as prepared by the method of Claim 55.
57. (Newly added) A method for preventing, treating, imaging or diagnosing of disease comprising administering the pharmaceutical composition as claimed in Claim 56 to a human.

58. (Newly added) A computer readable medium having thereon computer program code, wherein when said program is loaded onto a computer, the computer executes the method of Claim 32.

59. (Newly added) A computer program, distributable by electronic data transmission, comprising computer program code means adapted, when said program is loaded onto a computer, the computer executes the method of Claim 32.